UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,152	08/24/2001	Hisashi Narimatsu	2139.25	1765

5514 7590 05/20/2003

FITZPATRICK CELLA HARPER & SCINTO
30 ROCKEFELLER PLAZA
NEW YORK, NY 10112

EXAMINER	
RAO, MANJUNATH N	
ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/914,152	Applicant(s) NARIMATSU ET AL.	
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *14-25 and 28-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-47 are currently pending in this application. Claims 1-13, 26-27 are now under consideration. Claims 14-25, 28-47 remain withdrawn from consideration as drawn to non-elected invention.

Election/Restrictions

Applicant's election of Group I, claims 1-13, 26-27 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only. The correction requested for Figure 5 has been considered and entered.

Sequence Compliance

Applicant is required to comply with the sequence rules by inserting the sequence identification numbers of all sequences recited within the claims and/or specification. It is particularly noted that applicants have not provided SEQ ID NO depicted in specification for example see page 61, 66 or Table 4. See particularly 37 CFR 1.821(d).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7 and 8 are rejected because the invention appears to employ novel vectors. Since the vectors are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the plasmid but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance

or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide with SEQ ID NO:1 or the amino acid sequence comprising amino acids 31-310 of SEQ ID NO:2 and having ß 1,3-galactosyltransferase activity, does not reasonably provide enablement for such a polypeptide from any or all sources and for any variants, mutants or recombinants having the same activity but wherein one or more amino acids have been deleted, replaced or added to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-4 are so broad as to encompass any or all ß 1,3-galactosyltransferase from any source including variants, mutants and recombinants. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of ß 1,3-galactosyltransferases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity, requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the single nucleotide and encoded amino acid sequence of only one ß 1,3-galactosyltransferase. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides. The specification is limited to teaching making of the polypeptide with SEQ ID NO: 1 as ß 1,3-galactosyltransferase but provides no guidance with regard to the making of variants/mutants or provides no guidance with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide's primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification

fails to teach one of ordinary skill how to make/use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any or all ß 1,3-galactosyltransferases including any variants, mutants or recombinants having the same activity but wherein one or more amino acids have been deleted, replaced or added to SEQ ID NO:1, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the ß 1,3-galactosyltransferase activity, does not reasonably provide enablement for such a polypeptide from any or all sources and for any variants, mutants or recombinants having the same activity but wherein one or more amino acids have been deleted, replaced or added to SEQ ID NO:1. activity; (B) the general tolerance of ß 1,3-galactosyltransferase activity, to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any or all ß 1,3-galactosyltransferase amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any or all ß 1,3-galactosyltransferases with an enormous number of amino acid modifications of SEQ ID NOS: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of ß 1,3-galactosyltransferase polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 5-13, 26-27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DNA with SEQ ID NO:2 or DNA consisting of nucleotides 402 to 1331 or 492-1331 encoding a polypeptide with ß 1,3-galactosyltransferase activity, does not reasonably provide enablement for any or all DNA encoding such a polypeptide or any DNA hybridizing under stringent conditions to either DNA with SEQ ID NO:2 or DNA consisting of nucleotides 402 to 1331 or 492-1331 encoding a polypeptide with ß 1,3-galactosyltransferase activity or any DNA encoding a polypeptide with SEQ ID NO:1 having ß 1,3-galactosyltransferase activity wherein one or more amino acids have been deleted, replaced or added or fragments (oligonucleotides consisting of 5 to 60 nucleotides) of such DNA and derivatives of such fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 5-13, 26-27 are so broad as to encompass any DNA encoding a polypeptide with ß 1,3-galactosyltransferase activity or any DNA hybridizing under stringent conditions to either DNA with SEQ ID NO:2 or DNA consisting of nucleotides 402 to 1331 or 492-1331 encoding a polypeptide with ß 1,3-galactosyltransferase activity or any DNA encoding a polypeptide with SEQ ID NO:1 having ß 1,3-galactosyltransferase activity wherein one or more amino acids have been deleted, replaced or added or fragments (oligonucleotides consisting of 5 to 60 nucleotides) of such DNA and derivatives of such fragments. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNA sequences that are broadly encompassed by the claims.

The applicants propose to use the above polynucleotides for a variety of processes such as recombinant protein preparation, or as hybridization probes. Applicants also propose to use the DNA sequences in the form of oligonucleotide probes. Since the nucleotide sequence determines the type of protein and the ultimate function of the encoded protein and since only nucleic acids with very high percent homology can be used for recombinant protein preparation, or as hybridization probes, changing the nucleotide sequences as proposed by the applicants and/or addition of substantial amount of additional nucleotide sequence unrelated to the nucleic

acid sequence of SEQ ID NO:2 may not lead to desired function of the polynucleotides. This is because the changes suggested by the applicants will result in an enormous number of nucleotide sequences that will hybridize to several unrelated mRNAs instead of hybridizing specifically to mRNA of interest and similarly may hybridize to cDNAs totally unrelated to the cDNA of interest while screening a cDNA library. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of a single ß 1,3-galactosyltransferase from humans. It would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides. The specification is limited to teaching the making and using of the polynucleotide with SEQ ID NO:2 or 3 for encoding a ß 1,3-galactosyltransferase but provides no guidance with regard to the making of variants/mutants or provides no guidance with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polynucleotide's primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make/use the full scope of the polynucleotides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or modifications of nucleotides, as encompassed by the instant claims, and the base changes within a nucleic acid's sequence that can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited and the result of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given DNA to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all or any DNA sequences encoding ß 1,3-galactosyltransferase or encompasses modifications and fragments of any DNA encoding a ß 1,3-galactosyltransferase activity because the specification does not establish: (A) regions of the DNA sequence which may be modified without effecting the above mentioned activity/utility and used as fragments or probes; (B) the general tolerance of ß 1,3-galactosyltransferase DNA sequence to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleotide in the DNA encoding a ß 1,3-galactosyltransferase with an expectation of obtaining the desired biological function and utility; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any DNA or a fragment encoding ß 1,3-galactosyltransferase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of DNAs having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4 are directed to polypeptides having ß 1,3-galactosyltransferase. Claims 1-4 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including those derived from SEQ ID NO:1 and modified by at least one of deletion, addition, insertion and substitution of an amino acid residue in SEQ ID NO:2. No description has been provided of all the polypeptide sequences encompassed by the claims. No information, beyond the characterization of SEQ ID NO:1 has been provided by applicants which would indicate that they had possession of the claimed genus of polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences derived from SEQ ID NO:2, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structure. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 5-13, 26-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules encoding a protein with ß 1,3-galactosyltransferase activity.

The specification does not contain any disclosure of the structure of all DNA sequences encompassed by the claims. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed. Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-9, 12, 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Hennet et al. (J.Biol. Sci. Vol., 273(1):58-65, Jan. 1998). This rejection is based upon the public availability of a printed publication. Claims 1-6, 8-9, 12, 13 of the instant application are drawn to polypeptides having ß 1,3-galactosyltransferase activity involved in synthesis of sialyl-Lewis sugar chain, wherein the polypeptide consists of an amino acid sequence with SEQ ID NO:2 wherein the amino acids have been deleted, replaced or added, wherein the polypeptide activity is transferring galactose via ß 1,3-linkage to N-acetylglucosamine present at the non-reducing end of the sugar chain, wherein the polypeptides are encoded by polynucleotides capable of hybridizing under stringent conditions with SEQ ID NO:2, a recombinant DNA comprising said DNA, a host cell transformed with said DNA, wherein the host cell is a microbe, an animal cell or a plant cell, wherein the host cell is an insect cell such as *Spodoptera frugiperda* cell, a process of making the polypeptide by culturing the host cell in an appropriate medium and collecting the accumulated polypeptide. Hennet et al. disclose three polypeptides and their respective encoding polynucleotides, wherein the polypeptides have ß 1,3-galactosyltransferase activity and wherein such polypeptides can be considered variants resulting from either deletion, addition or replacing one or more amino acids in SEQ ID NO:1 and which polynucleotides are capable of hybridizing to the polynucleotide with SEQ ID NO:2 under stringent conditions. Examiner takes this position as the reference discloses an enzyme with identical activity. The reference also discloses host cells such as insect cells, *Sp.frugiperda* transformed with polynucleotides encoding the above enzyme and method of making the polypeptide by culturing said transformed cells. Since there is no limitation placed on the number of changes that can be present in the polypeptide sequence, SEQ ID NO:1, for a variant polypeptide and their respective

polynucleotides, claims 1-6, 8-9, 12, 13 read on the DNA sequence and the polypeptide disclosed by Hennet et al. Thus Hennet et al. anticipate claims 1-6, 8-9, 12, 13 of this application as written.

Claim 26 is rejected under 35 U.S.C. 102(b) as being anticipated by Kyowa Hakko et al. (GenBank Accession No. AAQ67067, 1995). This rejection is based upon the public availability of a printed publication. Claim 26 of the instant application is drawn to oligonucleotide having the same nucleotide sequence as a consecutive 5 to 60 nucleotide sequence of SEQ ID NO:2 or 3 or the polynucleotide of claim 5 (which is drawn to a polynucleotide that can hybridize under stringent conditions) or a derivative of the same. Kyowa Hakko et al. disclose a polynucleotide encoding a ß 1,3-galactosyltransferase or an oligonucleotide that has 100% match to 10-12 consecutive nucleotides of SEQ ID NO:2 (see enclosed sequence alignment). Therefore, Kyowa Hakko et al. anticipate claim 26 as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hennet et al. as applied to claims 1-6, 8-9, 12, 13 above, and further in view of the common knowledge in the art that *E.coli* and Chinese hamster ovary cells are two robust host cells that can be used for

expression of heterologous polypeptides. Claims 10-11 are drawn to a transformant according to claim 9, wherein the microorganism is *E.coli* or wherein the transformant according to claim 9 is an animal cell selected from a group consisting of CHO as one of the members.

The reference of Hennet et al. has already been discussed above. Hennet et al. disclose an insect cell as transformed cell. The reference does not teach or suggest the use of either *E.coli* or any mammalian cell as host cell. However, with the reference of Hennet et al. in hand, it would have been obvious to one of ordinary skill in the art wherein it is common knowledge that *E.coli* can be used as a very good host cell for quick small-to-medium-scale production of heterologous polypeptides and also that CHO cells which are adaptable for bulk growth are ideal for recombinant protein production of heterologous mammalian proteins, to use the DNA sequence taught by Hennet et al. and subclone it in appropriate vectors such that they can be used to transform either *E.coli* or the CHO cells and use them for production of the polypeptide. One of ordinary skill in the art would have been motivated to do so in order to make the polypeptide in bulk quantities for further characterization. One of ordinary skill in the art would have a reasonable expectation of success since Hennet et al. provide the polynucleotide encoding the polypeptide and art is rich in methods of transforming either *E.coli* or CHO cells.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kyowo Hakko et al. as applied to claim 26 above, and further in view of the common knowledge in the art for making derivatives of oligonucleotides such as oligonucleotides comprising phophorothioates.

The reference of Kyowo Hakko et al. as it applies to claim 26 has been discussed above. The reference teaches an oligonucleotide that is 10-12 nucleotides long and complementary to a portion of SEQ ID NO:2. However, the reference does not explicitly teach derivatives of such oligonucleotides.

With the above reference in hand it would have been obvious to one of ordinary skill in the art at the time the application was filed to make derivatives of such oligonucleotides using the vast number of techniques that are commonly available in the art. In fact, the art is so much evolved, that derivatives of known oligonucleotides can be ordered commercially. One of ordinary skill in the art would have been motivated to do so as it is well known in the art that these derivatives tend to be more stable than oligonucleotides as they are not degraded by nucleases found in cells or cell extracts. One of ordinary skill in the art would have a reasonable expectation of success since Kyowo Hakko et al. provide the oligonucleotide and methods to make derivatives are well known and available to those skilled in the art.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Manjunath N. Rao Ph.D.
Patent Examiner, A.U. 1652
5/16/03